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- (81) 指定国(国内): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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添付公開書類:  
— 國際調査報告書

2文字コード及び他の略語については、定期発行される各PCTガゼットの巻頭に掲載されている「コードと略語のガイドスノート」を参照。

(54) Title: MUTATED ANDROGEN RECEPTOR, CANCER CELLS EXPRESSING THE SAME, METHOD OF CONSTRUCTING THE SAME AND USE THEREOF

A1

(54) 発明の名称: 変異アンドロゲン受容体、それを発現する癌細胞、それらの作出方法およびそれらの用途

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(57) Abstract: It is intended to provide a mutated androgen receptor (AR) which are useful in screening a preventive/remedy for androgen independent cancer, etc.; DNA encoding the AR; and so on. It is also intended to provide a method of constructing a cancer cell line expressing the mutated AR *in vitro*; a method of screening an antiandrogen drug using the cancer cell line expressing the mutated AR obtained by the above method; a method of classifying antiandrogen drugs; a cocktail therapeutic comprising a combination of the antiandrogen drugs classified by the above method; and so on.

(57) 要約: アンドロゲン非依存性癌の予防・治療薬のスクリーニング等に有用な変異アンドロゲン受容体(AR)、該ARをコードするDNAなどを提供する。変異AR発現癌細胞株をインビトロで作出する方法、該方法により得られる変異AR発現癌細胞株を用いた抗アンドロゲン剤のスクリーニング方法、抗アンドロゲン剤の分類方法、該方法により分類された抗アンドロゲン剤を組み合わせたカクテル療法剤などを提供する。

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP03/06942

## A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl<sup>7</sup> C12N15/12, C07K14/72, C07K16/28, C12N5/10, C12P21/02,  
 C12P21/08, C12Q1/02, A61K38/17, A61K39/395, A61K48/00,  
 A61P35/00, G01N33/15, G01N33/50, G01N33/53, G01N33/566

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl<sup>7</sup> C12N15/12, C07K14/72, C07K16/28, C12N5/10, C12P21/02,  
 C12P21/08, C12Q1/02, A61K38/17, A61K39/395, A61K48/00,  
 A61P35/00, G01N33/15, G01N33/50, G01N33/53, G01N33/566

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 SwissProt/PIR/Geneseq, WPI (DIALOG), BIOSIS (DIALOG), MEDLINE (STN)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	Sadar, M.D. et al., Androgen-independent induction of prostate-specific antigen gene expression via cross-talk between the androgen receptor and protein kinase A signal transduction pathways., J.Biol.Chem., Vol.274, No.12, pages 7777 to 7783, (1999)	1-10, 12, 18-28 50-55, 60
X A	Veldscholte J. et al., A mutation in the ligand binding domain of the androgen receptor of human LNCaP cells affects steroid binding characteristics and response to anti-androgens., Biochem.Biophys.Res.Commun., Vol.173, No.2, pages 534 to 540, (1990)	1-10, 12, 29-43, 59 50-55, 60

 Further documents are listed in the continuation of Box C. See patent family annex.

## \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search  
29 August, 2003 (29.08.03)Date of mailing of the international search report  
16 September, 2003 (16.09.03)Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP03/06942

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Taplin M.E. et al., Selection for androgen receptor mutations in prostate cancers treated with androgen antagonist., Cancer Res., Vol.59, No.11, pages 2511 to 2515, (1999)	9,10,12, 29-43,62
X	Marcelli M. et al., Amino acid substitutions in the hormone-binding domain of the human androgen receptor alter the stability of the hormone receptor complex., J.Clin.Invest., Vol.94, No.4, pages 1642 to 1650, (1994)	29-41,50-55, 60 62
A	US 6291194 B1 (Taneli Raivio), 18 September, 2001 (18.09.01), & WO 02/10762 A1 & EP 1305630 A1	9,10,12
Y	Gaddipati J.P. et al., Frequent detection of codon 877 mutation in the androgen receptor gene in advanced prostate cancers., Cancer Res., Vol.54, No.11, pages 2861 to 2864, (1994)	29

**INTERNATIONAL SEARCH REPORT**

International application No.

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**Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 16, 46, 47, 61, 64, 66

because they relate to subject matter not required to be searched by this Authority, namely:

The inventions as set forth in these claims pertain to diagnostic or therapeutic methods for treatment of the human body.

2.  Claims Nos.: see below

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Since compounds specified exclusively by a screening method or a function are described in claims 11, 13 to 15, 17, 44, 45, 48, 49, 56 to 58, 63 and 65, these claims involve any substances obtained by the method or any substances having the function in the scopes thereof.  
(continued to extra sheet)

3.  Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Since a method of screening an androgen receptor (AR) ligand using a cell line expressing a mutated AR had been publicly known before the priority date, the inventions as set forth in claims 20 to 28 relating to a screening method using a PSA promoter and the inventions as set forth in claims 62 to 66 relating to a method of classifying antiandrogen drugs cannot be considered as relating to a group of inventions so linked to other inventions as to form a single general inventive concept. Such being the case, the claims of the present case have 3 groups of inventions.

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest  The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.  
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Continuation of Box No. I-2 of continuation of first sheet (1)

However no specific substance is presented in the description. Thus, claims 11, 13, 15, 17, 44, 45, 48, 49 and 56 to 58 are neither supported by the description nor disclosed therein. Also, these claims are described in an extremely unclear manner.